

THE CHANGES IN THE NERVOUS SYSTEM WHICH FOLLOW
UPON AMPUTATION OF THE LIMBS.

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In this thesis I propose to give, in chronological order, an account of the observations recorded in the literature of my subject, to illustrate them by means of drawings from sections of the spinal cords of amputated patients and others, and, finally, to discuss the facts reported and the various theories which they have been held to support.

The drawings were made by me from sections which I prepared in the laboratory of Professor Marie in the Bicêtre Hospital at Paris. The drawings were produced by means of an apparatus which cast a magnified image of the section - stained by Weigert's method - upon the drawing sheet, so that its outlines could be readily and accurately reproduced. The reality of the scleroses demonstrated by the method of Weigert was confirmed by the subsequent staining of similar sections by the method of Van Gieson. To Professor Pierre Marie my thanks are due for his

courtesy and kindness in supplying me with the necessary material.

As early as 1829 the question of changes in the nervous system consecutive to amputation of the limbs attracted the attention of Bérard, who published a case in which he had noted atrophy of the anterior spinal roots supplying the amputated member. His observations, however, are of doubtful value.

In 1868 Vulpian published several investigations. In his first two cases he found no alteration in the nerves, although amputation had occurred in one case 47, and in the other 20, years before death. In a case of section of the sciatic nerve of five months standing he found no alterations in the proximal part of the nerve beyond a thinning of some of the fibres. In none of his cases did he observe any alteration of the nerve roots. In the spinal cord, however, he found changes both in the white matter and in the grey. In two cases of amputation with autopsy after the lapse of 2 and 10 years respectively, he observed a) in the first, an atrophy of the anterior column of white matter and the anterior horn of grey matter on the side of the lesion, together with a diminution in the number of ganglion cells in the affected anterior horn, particularly in its antero-lateral

group, and b), in the second an atrophy of the posterior horn and of the posterior and lateral columns of white matter on the side of the amputation. In three cases of amputation of the lower limb dating back 16, 20, and 47 years respectively, he observed likewise a unilateral affection of the cord on the side of the amputation; in the first, there was a diminution of the posterior column, in the second a diminution in the anterior and posterior columns and in the posterior horn, and in the third a diminution in the anterior column and in the grey substance generally. In none of these cases were there any alterations in the ganglion cells. He found no qualitative alteration of the elements present with the single exception of a case in which he noted the "pseudo-lacunary degeneration" of the grey substance described by Lockhart Clarke in certain cases of muscular atrophy.

Dickinson on the contrary in the same year as Vulpian observed in two cases of amputation through the thigh, and in two cases of amputation of the upper arm, the two latter being of 23 years' standing, a high grade of atrophy of the spinal nerves going to the affected limb, and attributed it to a diminution of the number of fibres. In the spinal cord in all four cases he noted a decided diminution of

the posterior column on the corresponding side, particularly in the neighbourhood of the grey commissure, together with a slight degree of sclerosis. In the two arm cases there was likewise an inconsiderable diminution of the grey substance without any alteration of the ganglion cells. In one of the arm cases the posterior roots on the same side in the lower portion of the cervical region were decidedly diminished and in a high degree "degenerated", while, in the corresponding anterior roots only a trace of these changes was to be seen.

In 1873 Friedreich examined the cord of a woman aged 37 amputated through the left arm 12 years previously. He found no changes whatever. In the same year Dickson in a case of amputation of the arm of 15 years standing observed a diminution in the corresponding anterior horn with a diminution in number and an atrophy of its ganglion cells.

In 1875 and 1876 Hayem published an account of researches upon young rabbits, in which the sciatic nerve was torn away and a rapid atrophy followed in the nerve cells of the postero-lateral group in the anterior horn; as well as two communications regarding the changes in the nervous systems of amputated patients proper. In these last he found an atrophy of the fibres in the central portion of the

nerves. He noted no trace of degeneration, but in the nerve of the stump there were numerous very fine nervous fibres grouped in bundles which he regarded as newly formed nerve fibres. He observed further that after the lapse of 25 years these small fibres were larger than after 5 years. In the cord he described an atrophy of the corresponding posterior column and posterior horn, and in one case of amputation of 5 years' standing an atrophy in the anterior horn alone with diminution in the number of ganglion cells.

In 1876 Leyden described in 3 cases of $2\frac{1}{2}$, 3, and 5 years' duration respectively, an atrophy of the whole corresponding half of the cord; the principal changes, however, were in the anterior and antero-lateral columns of white matter, and there was no diminution of the ganglion cells in the anterior horn.

In the same year Genzmer investigated the case of a woman amputated through the inferior third of the thigh on account of a caries of the knee-joint. Death occurred 30 years later. The only changes noted were a diminution in size of the anterior roots and the anterior horn in the lower half of the lumbar enlargement, while the ganglion cells of the horn were strikingly reduced in number.

In 1878 Déjérine and Mayor described in the

cases which they examined an atrophy of the affected nerves, which became less obvious as these were ascended towards their origin, and disappeared at a distance from the spinal ganglions. In the spinal roots they noted no alterations. As regards the cord, however, in 3 cases of 4, 5, and 9 years' duration respectively, they observed an atrophy of the entire corresponding half of the cord without any reduction in number of the ganglion cells in the anterior horn. In 4 cases of amputation through the thigh of 17, 22, 23, and 30 years' duration respectively, and in one case of disarticulation at the shoulder-joint of 40 years' duration, they described an atrophy spread equally over grey and white substance. In the case of 30 years' duration alone the ganglion cells in the anterior horn were diminished in number by a third, and particularly in the antero-median group.

In 1879 Dreschfeld in a case of 15 years standing found no changes in the nerves or roots, but an alteration in the cellular groups of the corresponding anterior horn, especially in the posterolateral group, consisting in a diminution of their volume with a reduction in their number, besides a slight atrophy in the posterior horn.

In 1880 Erlitzky described in young dogs after amputation a thinning of the posterior column and

posterior horn on the side of the lesion, with a reduction in number and size of some of the nervous cells in the anterior horn.

In an adult dog, however, deprived of one of its hind limbs two years previously, he found no alterations whatever in the cord.

In 1880 Brown Sequard described a unilateral atrophy of the spinal ganglions corresponding to a section of the sciatic nerve.

In the same year Kahler and Pick described two cases. In the first of these of six years' standing they found an atrophy of the corresponding posterior column, and posterior part of the lateral column, and an atrophy of the anterior horn with reduction in number of its ganglion cells, especially in the outer lateral group. In the second case, an amputation through the inferior third of the left thigh with death from potassium cyanide poisoning 18 years later, they found a marked atrophy of the corresponding anterior and posterior columns, and a reduction in number of the ganglion cells in the anterior horn especially in the middle group.

In 1882 Edinger observed a case of intra-uterine amputation of the hand and the greater part of the forearm. Death occurred from heart failure at the age of 52. In the corresponding portion of the cord he found atrophy of the white and grey substance es-

pecially of the anterior horn. The atrophy extended from C. 4 to D.2, but the changes were most marked in C. 6, and C. 7, where there was a considerable diminution in number as well as an atrophy in the ganglion cells of the anterior and posterior outer projections of the horn. The peripheral nerve trunks and anterior and posterior roots showed likewise a considerable diminution. In three cases of ordinary amputation he noted atrophy of the whole corresponding half of the cord, the principal changes occurring in the anterior horns.

In 1884 Hayem and Gilbert published a note on the modifications which occur in these cases. In the central ends of the nerves they found atrophy of most of the fibres consisting in a simple disappearance without any sign of degeneration. However they observed occasionally a true hypertrophy of certain fibres. They explained these appearances as the result of a re-formation of previously degenerated fibres. The roots of the nerves, both anterior and posterior, they found to be similarly affected on the side of the lesion. In the cord they found an alteration both of the white and the grey matter, a diminution in volume, namely, of the posterior column on the side of the lesion, and a diminution of the grey substance in both the anterior and posterior

horns on the same side including an atrophy of some cellular groups in the anterior horn. The changes consisted throughout, not in a reduction of number, but in a reduction of volume in the elements themselves, although certain cells are described as having a form more globular and massive than ordinary.

The observations of Dufley Wiglesworth and Reynolds in 1886 and 1887 are not of much value as their subjects had suffered from well-marked nervous diseases.

In 1886 Friedländer and Krause published observations, founded on the study of 8 cases, which are among the most remarkable of those recorded in the earlier literature of the subject. Of these, 4 were amputations through the thigh of 10, 5, 4, and several years' duration respectively. Two were amputations through the leg of three months, and several years' duration respectively, and 2 were amputations through the upper arm of 3 and 8 years' duration respectively. It may be noted that Friedländer and Krause were the first to employ the method of Weigert in this connection.

As regards the nerves, they found in every case a change in a considerable proportion of the fibres which they described as consisting at once of simple atrophy and of Wallerian degeneration. The affected

fibres formed islets, which, according to these authors, corresponded to the primitive nerve-fibre bundles into which a normal nerve-trunk is divided up. The degenerated islets usually included one or several normal nerve fibres, slender or broad as the case might be. The modifications in the affected fibres consisted in alterations of the medullary sheath, which had lost its normal sheen (Fett-glanz) and its colour reactions, and of the axis cylinder which had become a shadowy structure. The atrophic fibres, therefore, had a certain similarity to non-medullated fibres without however being identical with them. Moreover non-medullated nerve fibres are extremely scanty in normal nerve-trunks. The atrophy thus differed from the acute destruction of sheath and cylinder which occurs in ordinary Wallerian degeneration within a short time; after amputation there remained for microscopical examination a distinct residue of each fibre. Among the atrophied nerve bundles a multiplication of nuclei was easily demonstrable. New formation of nerve fibres was not observed, and it appeared to these authors that the number of atrophied nerve fibres corresponded to the number of healthy fibres previously present. Finally, this atrophy of nerve fibres was already fully evident three months after amputation, although the fi-

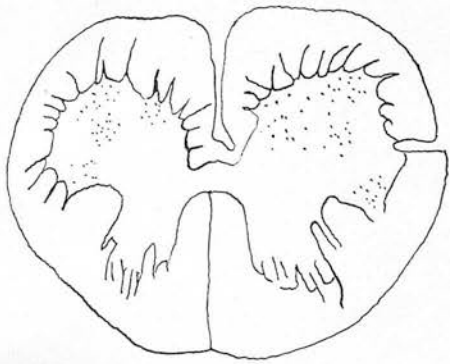
bres did not then appear so thin as in cases of later date. The alteration was similar from top to bottom of the nerve and extended upwards as far as the intervertebral ganglia. Friedländer and Krause were of opinion that these changes escaped notice previously owing to the insufficiency of earlier methods of research. They noted, however, that not all the sensory fibres from the amputated limb were atrophied, but only a part, and that everywhere in the nerve and almost in every one of their atrophic primitive bundles some normal medullated fibres, broad as well as narrow, were to be found. This was true both of the sciatic and also of purely sensory nerves and they admitted the unlikelihood of its resulting from intermixture with fibres from the central unsevered branches. As the trunk of the nerve was ascended the atrophy naturally became less marked in proportion to the entire cross-section, and assumed a central position. Fibres joining the nerve from branches above the level of the amputation they found to be intact on the whole. On examination of the spinal roots immediately below the ganglions where the motor and sensory roots are still separate from each other, they found the atrophy to be limited almost entirely to the sensory roots and to present the same patchy appearance as in the mixed nerves

except that the atrophied parts occupied proportionately more of the cross-section. Even here, however, normal nerve fibres were to be seen within the supposed atrophied bundles. The atrophy of the sensory nerves was thus not complete. The anterior roots were in every case normal in appearance. The atrophy thus limited to the sensory fibres stopped short however at the ganglions and above these both the anterior and the posterior roots were normal.

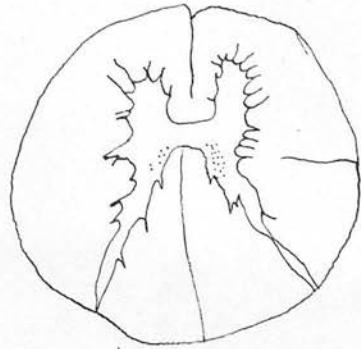
Their observations upon the changes in the spinal cord were equally definite. In every case they found a diminution in size of the posterior column on the side of the amputation. In amputations of the lower limb the diminution commenced in the lower portion of the lumbar enlargement, increased up to the 8th dorsal segment, where it was usually most marked, and then decreased towards the cervical region, where, however, it was easily demonstrable as a rule. The alteration consisted in a purely quantitative defect, except that a slight increase in nuclei might perhaps be noted. This increase was considered as probably apparent rather than real, being most marked where the diminution in volume was greatest, that is anteriorly near the grey commissure. A

moderate diminution of the grey matter was noted in the corresponding posterior horn, but only in the lower segments of the cord.

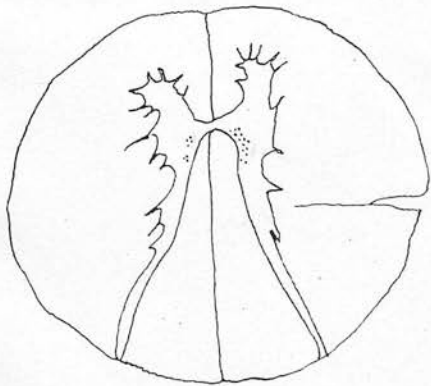
Finally as regards the ganglionic columns of the grey matter two changes were noted. The anterior horn on the side of the lesion in that part of the cord where the sacral nerves take origin, i.e., in the middle of the lumbar enlargement, was decidedly diminished in size and especially in its lateral portions. Exact enumerations were accordingly made, in a series of sections, of the cells in the antero-median, antero-lateral, central and postero-lateral groups, and it was found that the number of cells in the postero-lateral group on the unaffected side was between two and three times greater than the number of the corresponding cells on the side of the amputation. It may be noted here in regard to this point that the same result was observed by Mayor and Van Gudden in experiments on newly born rabbits deprived of the sciatic nerve by section or tearing away. Lastly Clarke's column on the amputated side showed a diminution in the number of its ganglion cells from the 12th to the 6th dorsal segment, and in one case to the 5th dorsal segment. In neither of these two cell groups could a diminution in nerve fibres be demonstrated. In the single case of amputation through



Section of cord (middle part of lumbar enlargement) in a case of amputation of the left lower limb. — Remark that the left half of the cord is in almost every part, & notably in the posterior column & in the anterior horn, of less dimensions than the right half. (The incision in the right lateral column was made previous to hardening in order more easily to orient the sections.)



Section of the Cord (Inferior Dorsal Region) in a case of amputation of the left lower limb. — The left half of the cord is smaller than the right, the cells of the column of Clarke are of less number.



Section of Cord (middle dorsal region) in a case of amputation of the left lower limb. — Left half of cord smaller than right, cells of left column of Clarke less numerous than those of right.

the arm examined by the authors there was very marked diminution of the posterior column on the side of the lesion in the whole cervical region, and the posterior horn was likewise diminished but in less degree.

As a result of their observations Krause and Friedländer drew the following conclusions: -

- 1) That the changes following on amputation are found only in the sensory system;
- 2) That the changes in the nerves consist in a peculiar degeneration;
- 3) That only a portion of the sensory fibres in the nerve are affected, and they suppose therefore that only certain kinds of nervous fibres atrophy, namely those which terminate in specific end-corpuscles.

The facts which they urge in support of these conclusions are as follows: -

- 1). There was almost as much alteration to be observed in the nerves in the case of amputation above the malleolus as in a case of thigh amputation, a fact which they explained by the occurrence of the specific nerve endings chiefly in the sole of the foot, and in the toes in accordance with the sense

of touch. In this view not the loss of function but the loss of cellular apparatus would be the cause of the atrophy.

2) An analogy to the process might be found in the ascending atrophy of the optic nerve which follows destruction of the bulbus oculi.

This supposed specific atrophy reached only to the spinal ganglions; above these, numerical diminution only occurs. The atrophy is similarly numerical, though here clearly evident, in the corresponding posterior column. The atrophy in the two groups of ganglion cells above mentioned found its analogue according to these authors in the atrophies of central organs after extirpation of peripheral structures studied by Gudden.

In a later publication Krause identified in essence with Wallerian degeneration the degenerative processes in the nerve trunk.

For the sake of convenience I may note at this point the only two facts about which the investigators previously cited are practically agreed. Namely, first, that the lesions are invariably unilateral and correspond in this respect with the amputations which preceded them, and secondly, that their situation in the case of amputations of the lower limb is in the lumbar enlargement although different views are

expressed as to the height to which the atrophy ascends.

In 1890 Homén published his researches upon dogs of two or three weeks old in which disarticulation at the knee or hip had been performed and the dogs afterwards allowed to live for periods varying up to five years. Within half a year a very high degree of atrophy was noticeable in the cord, but after that period further alteration was slight. Relatively soon after the operation changes were found in the peripheral nerves, but it was only after some time that these changes, spreading from below upwards, affected the different parts of the corresponding region of the cord, and only after years that changes were noted in the ganglion cells of the anterior horn. The changes described in the peripheral nerves resembled those described by Friedländer and Krause, and were similar to those of Wallerian degeneration, from which however they differed in intensity and distribution. They consisted in a loss of coloration by Weigert's method in the myelin sheath, a considerable thinning of it, and, in the case of some fibres, its complete disappearance. There was further an increase in the nuclei, and, finally, in the degenerated fibres, the axis cylinder was eventually destroyed. In contradistinction to Friedländer and Krause, however, Homén emphasized the absence of any particular

arrangement of the healthy and unhealthy fibres in the nerve. He observed in addition that a growth of connective tissue followed, but only in a relatively short portion of the nerve in the amputation stump. Like Friedländer and Krause, and on similar grounds, he arrived at the conclusion that the atrophy in the nerve trunks affected the sensory fibres only. He also described appearances indicative of degeneration in the corresponding spinal ganglia, particularly in their peripheral portion. Macroscopically the intervertebral ganglia corresponding to the amputation appeared diminished by about one third as compared with those of the opposite side. In agreement with Friedländer and Krause he believed that the spinal ganglion cells exercised in accordance with their well-known trophic function a counteracting influence upon the ascent of the degeneration. He noted however in the posterior roots above the ganglion a very small number of fibres which presented a degenerated appearance, and considered this observation to be in favour of the existence of fibres whose trophic centres were not in the ganglion, but in the spinal cord. As regards the changes in the spinal cord he found a diminution in the posterior column and in the posterior horn on the side of the amputation best marked in the enlargements of the cord and particularly in the lum-

bar enlargement. The diminution in the posterior column proceeded so far as to reduce it by one half. In the posterior horn it was not so marked. He found also a diminution in the lateral part of the anterior horn. Here the ganglion cells were reduced in number as were also the cells of Clarke's column on the same side. He found in addition atrophic changes in the remaining cells in these regions. In amputations at the knee he found the changes were less marked than in amputations at the hip. It will be seen that the observations of Homén coincided with those of Friedländer and Krause to a great extent. He, however, emphasized the fact that alterations occur in the motor sphere as well as in the sensory although in a much less considerable degree and after a longer lapse of time. According to him, the motor changes consisted in a slight diminution in number as well as in an atrophy of the ganglion cells of the anterior horn, and in a barely noticeable reduction in size of the anterior roots.

In 1891 Vanlair followed Homén with the publication of a number of observations upon the effect upon the nervous system of experimental section of nerves, and amputations in the adult dog. In ten cases of section of the sciatic nerve, followed by complete, or almost complete, regeneration, with

autopsy after periods varying from six months to $2\frac{1}{2}$ years, he found in the central end of the divided nerve a relatively considerable number of fine fibres with a reduction in volume of the myelin sheath and of the cylinder axis, but especially of the former.

These fine fibres as a rule formed compact bundles disseminated amongst fibres of ordinary dimensions. They became gradually scarcer towards the origin of the nerve and finished by disappearing, or rather by becoming reduced to an ordinary number near the point of emergence of the nerve. A similar appearance had already been noted by Déjérine and Mayor. These fibres were most obvious in the earlier autopsies (six months). There was no appearance of degeneration, but the fibres took a less accentuated colour with osmic acid - a circumstance mentioned by Ranvier in connection with newly regenerated nerve fibres. The spinal roots were intact in every case and the cords showed no sign of asymmetry.

In three animals only were changes found in the cord. In one case of bilateral division of the sciatic with autopsy $2\frac{1}{2}$ years later, a lesion was found in the lumbar region. "Independently of an obvious "ectasis of the central canal and a thickening of the "muscular layer of the peri-ependymal arteries - a "thickening which Lockhart Clarke had recently remarked in certain cases of progressive amyotrophy - there

"existed a very manifest lesion of the left anterior
"horn, whose central group was degenerated. The
"ganglion cells had disappeared as such and had passed
"into the state of formless corpuscles massive, op-
"aque, and deprived of their prolongations and of
"any appearance of a nucleus. The nervous fibres of
"the horn and even the neuroglial elements had like-
"wise undergone complete disintegration. The degen-
"erated focus occupied the extreme inferior portion
"of the lumbar enlargement and its longitudinal di-
"mensions did not exceed a centimetre."

In a second case of bilateral division of the
sciatic nerves, repeated and followed by normal re-
production, there was found "a dilatation, without
"thickening of their walls, of the peri-ependymal ar-
"teries in the lumbar enlargement and slightly also
"in the inferior part of the dorsal cord."

In the third case after simultaneous section of
both sciatics and a year later section of the left
sciatic followed by autopsy in six months there was
found "an atrophy of the left posterior horn. It
"appeared at once narrower and shorter than its com-
"panion; the cells seemed smaller than on the other
"side, but without any sign of degeneration. The
"posterior column on the left side and the posterior
"portion of the left lateral column also appeared

"diminished without presenting, however, any appreciable structural lesion. The postero-lateral group on the left side compared to that on the right showed an evident nuclear multiplication." The lesion then so far as the nervous structures were concerned was a purely atrophic one.

In three cases the sciatic was severed and regeneration of the nerve was prevented. One of these examined 9 months later showed an increased number of fine fibres in the central end of the trunk without any change in the roots or cord. The second case, examined after 9 months gave the same results. The third case examined at the end of two months gave likewise the same results, with this difference only that the fine fibres in the central end of the nerve appeared more numerous than in the two previous cases.

To sum up: the operation of section produced in the central end of the divided nerve the appearance of a relatively considerable number of fasciculated slender fibres. Unilateral section of the sciatic produced no further results. Bilateral section with later reproduction was followed in two cases by changes in the medullary substance, but these were not uniform. It may be noted that though both sciatics were divided, the lesion was unilateral in each instance. A series of nine amputations was

now undertaken.

Experiment 1. Amputation of the right hind limb through the superior part of the thigh. Autopsy after 3 months.

Result: No change in the roots or cord. The nerves were not examined.

Experiments 2, 3 and 4. Amputation through the middle of the right leg. Autopsy after 2, 5½ and 10 months respectively.

Result: An increase in slender fibres in the nerve up to the middle of the thigh. The roots and cords were normal.

Experiments 5 and 6. Amputation half way between toes and heel of right foot. Autopsy after 4 and 7 months respectively.

Result: Roots and cords normal.

Experiment 7. Amputation through the superior portion of the right thigh, following on a section, performed three days previously, of the right sciatic nerve near its point of emergence into the leg. Autopsy after 6 months.

Result: Roots and cord normal.

Experiment 8. Amputation through the middle of the right thigh. Autopsy after 8 months. Note that some days before its death the animal was seized with a spastic paralysis of the left

hind limb, that is to say on the side opposite to the amputation, which forced it to creep behind upon its quarters.

Result: 1) Examination of the nerves. Apart from a manifest multiplication of slender fibres either isolated or united in bundles, which was found reaching upwards to the point of emergence of the nerve, no alteration was discovered in the right sciatic. The left sciatic was normal.

2) Examination of the Nerve Roots: In the inferior portion of the dorsal region on the right side the roots both anterior and posterior were atrophied to about the same degree but without any appearance of degeneration. The relation between a right and a corresponding left root was as 1 to 1.5 approximately.

3). The Cord: The right antero-lateral column of white matter as compared with the left was manifestly reduced in size in an average proportion of 1 to 1.35. The lateral zone had undergone the greatest diminution. The posterior columns were equal in size. The right anterior horn was shorter than the left in the proportion of 1 to 1.2, and narrower in the proportion of 1 to 1.3. The thickness of the reticular process on the right side was equally diminished as compared with the left. The

posterior horns right and left were of the same size and the column of Clarke was intact.

In spite of this asymmetry of the entire antero-lateral system there was no textural alteration anywhere. The modifications just cited occupied the middle and inferior portions of the dorsal region. In the lumbar region the cord appeared normal.

Experiment 9. Amputation through the superior portion of the right leg, combined with enervation of the stump (resection of the saphenous and the right sciatic in the middle of the thigh). Autopsy after 15 months. Paralytic and spasmodic accidents occurred during life, affecting especially the left limb and extending to the forelimb and the face, but no asymmetry nor any alteration of the elements of the cord was determined after death. "There existed only a marked thickening of the walls of the periependymal vessels in the lumbar enlargement. The sciatic nerve presented as usual a multiplication of slender fibres up to a certain height, but nothing more.

Finally, in several of the above cases a number of ganglia were examined at different levels without result.

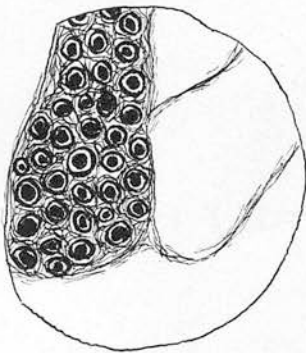
Vaulair summarized his results as follows. Out of nine amputations only one showed an alteration of

the cord on the side of the lesion, " a purely numerical atrophy localised in a part of the dorsal region." He concluded that neuro-medullary atrophy appeared to be an accidental complication of the operation, at least in healthy adult animals. He admitted, however, that neuro-medullary changes were proved in man and suggested that some at least of them might be due rather to the surgical affection which necessitated amputation in the first instance, than to the amputation itself.

In 1891, subsequently to the experiments of Vanlair, Pierre Marie published the results of his investigations into the question. As regards changes in the nerves he described an extensive degeneration of the fibres in the central portion of the divided nerves. In illustration of this he selected a case of amputation through the middle of the left thigh, in which the operation preceded death by twenty years. At autopsy the left sciatic nerve was found to be nearly double the size of the right, the increase in volume tending to diminish towards the spinal column. This change had been mentioned by several authors, but the degree of its inconstancy may be judged of from the account given by Hayem and Gilbert of a case of amputation of the arm, in which it is stated that the radial

nerve was slightly diminished on the affected side, that the ulnar gradually increased from the brachial plexus to the terminal neuroma, near which it was twice the size of the sound nerve on the opposite side, while the median nerve was of the same dimensions on both sides.

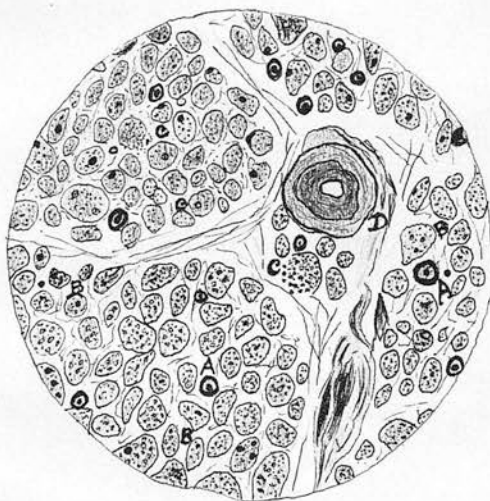
In Marie's case, on section of the nerve, it was found to be extensively degenerated, the myelin having completely disappeared from the greater part of of the section. In contra-distinction to the findings of Krause and Friedländer the primary islets were larger than normal and the partitions between them were broadened and presented a myxoid appearance. The blood vessels, however, were not increased in number and their walls were only moderately thickened. A few primary islets were filled, as in a healthy nerve, with a mosaic of closely set medullated fibres, but in contrast to these the great majority presented a degenerated appearance, the myelin having disappeared and the nerve fibres being replaced by "islets of degeneration" with a diameter of about three or four times that of a normal fibre and distended with fine fibrils. The adjoining figures from Marie's "Leçons sur les Maladies de la Moëlle" (tracings) give a good idea of the change. Marie believes these small degenerated islets to be identical with the so-called degenerated primitive islets of



Fragment of a section of a healthy sciatic nerve, showing the tracts of connective tissue which separate the "primitive islets". Section coloured with Weigert's Haematoxylin. The nerve fibres are drawn in one "islet" only.

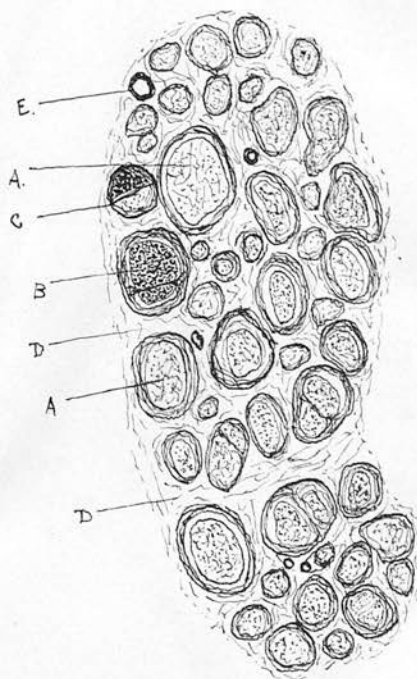
After Marie, Maladies de la Moelle. 1892 p. 71

D, vessel with thickening of walls (notably exaggerated in the drawing). The segments isolated by white tracts are the "primitive islets". (After nature, semi-schematic, Weigert-Staining.)



Fragment of section of left sciatic nerve in a case of amputation of the left thigh dating from 20 years back. A, A, A, normal nervous fibres conserving their cylindrical axis & myelin sheath.

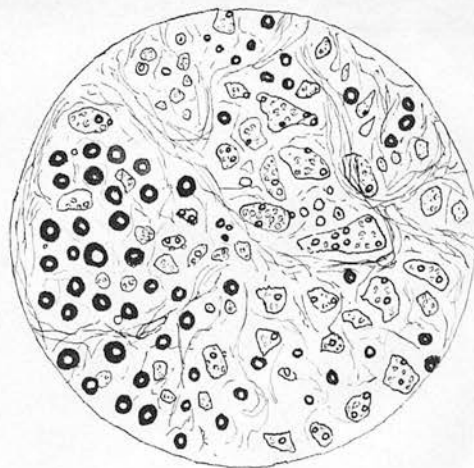
B, B, B, islets of degeneration of rounded or polyhedral form & containing in their interior fairly numerous fine points which are fine nervous fibres of regeneration; in some are seen several black points which indicate the presence of several fine fibres with myelin. C, C, islet of degeneration whose boundary is broken & whose fine fibres escape & separate from one another.



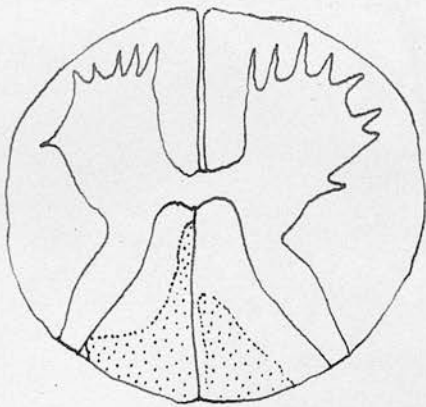
Section of the left sciatic nerve in a case of amputation of the left thigh dating from 20 years previously:

A: Degenerated primitive bundle; B normal primitive bundle; C primitive bundle of which 1/2 is degenerated the other half normal; D Interfascicular trabeculae with myxoid aspect; E. Vessel.

Krause & Friedländer



Fragment of nerve in case of amputation.

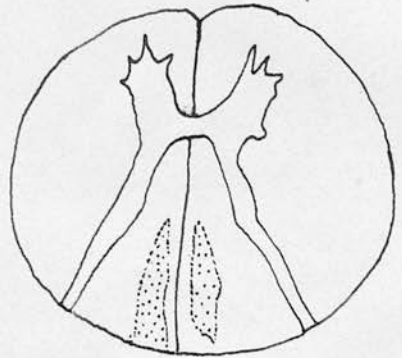


Section of cord in lumbar region in case of amputation of left thigh dating back 20 years:—

In left posterior column a zone of degeneration.

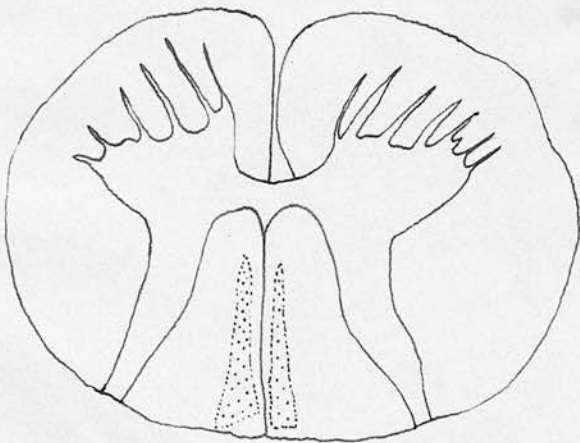
In right posterior column a second zone of degeneration but less pronounced and of less extent. — It will be remembered that the zone of degeneration on the left side is contiguous posterio-externally to the posterior horn, which seems to indicate that it is due to degeneration of posterior root fibres situated below the level of the section. The diminution in volume of left half of cord is very marked.

(Diagrammatic tracing:— Degeneration indicated by dotted areas.)



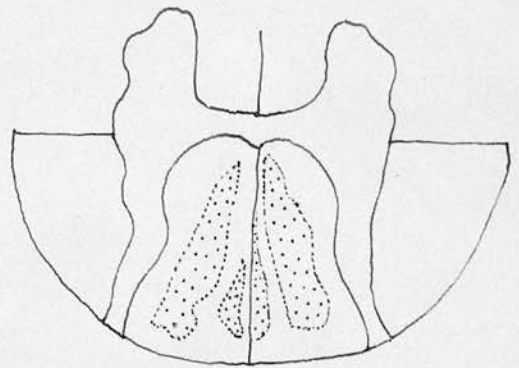
Section of cord in dorsal region, in same case:—

The zone of degeneration is here much nearer the postero-median septum and is clearly situated in the column of Goll. The diminution in volume of left half of cord is very marked.



Section of cord in cervical region in same case:—

The zones of degeneration were much less marked and of much less extent than in the dorsal or lumbar sections. The diminution in volume of the left half is less marked than in the other sections.



Section of cord in cervical region in case of amputation of right arm. In the posterior columns on either side there existed two zones of degeneration separated by a band of healthy tissue. The degeneration was more manifest on the right side.

at repair, may be of septic origin, whatever its actual mechanism was.

He disagrees with the statement of Friedländer and Krause that in amputations above the malleolus degenerated fibres are as numerous in the nerves as in amputations through the thigh. According to his own observations in such a case degenerated fibres are few in number.

Finally then he is of opinion that in the nerves two processes may have been operative, Wallerian degeneration and an ascending neuritis.

Secondly, in regard to the alterations in the spinal cord: he is of opinion that asymmetry in the cord is frequent but not usually present to the degree which is found after amputation. He believes in a direct relation between the amputation and the atrophy, and he concludes that the posterior column is the portion of the cord which is most constantly affected and in the most pronounced way.

He believes further that the fibres of the two posterior columns intercross with each other to a certain extent and in this way the occurrence of sclerosis on both sides of the postero-median septum is explained. In this connection he refers to the experiments of Tooth, Oddi and Rossi, who, having made a section of some of the posterior roots upon one side of the cord, observed a degeneration in the

posterior column on the opposite side. His opinion as regards the origin of the sclerosis itself has already been mentioned.

In 1892 Marinesco published the results of a careful examination of three cases. His first case was that of a man, amputated through the left thigh at the age of 30 years, who died twenty one years later of paralytic dementia following upon an apoplexy. In the cord he observed an asymmetry, particularly in the lumbar enlargement, due to a diminution in size of the posterior column on the side of the amputation, and an atrophy of the grey substance on the same side, especially of the anterior horn. Macroscopically, the posterior roots appeared thinner on the left side than on the right. The atrophy of the anterior and posterior horns diminished gradually from below upwards in the lumbar enlargement, and disappeared entirely in the dorsal region, to reappear, in the anterior horn only, in the cervical. The atrophy of the white substance in the dorsal and cervical cord affected Goll's column only, but was clearly distinguishable throughout.

The column contained further a trace of degeneration.

The changes in the sacral cord affected especially the anterior and posterior horns. In this

region the number of ganglion cells in the postero-lateral portion of the anterior horn was very much diminished in the proportion 232 (on the sound side) to 82. The postero-lateral group of ganglion cells in the lumbar region was likewise diminished in the proportion 375 - 114. The other ganglion cell groups in these two regions were likewise affected to a noticeable though less extent by the atrophy.

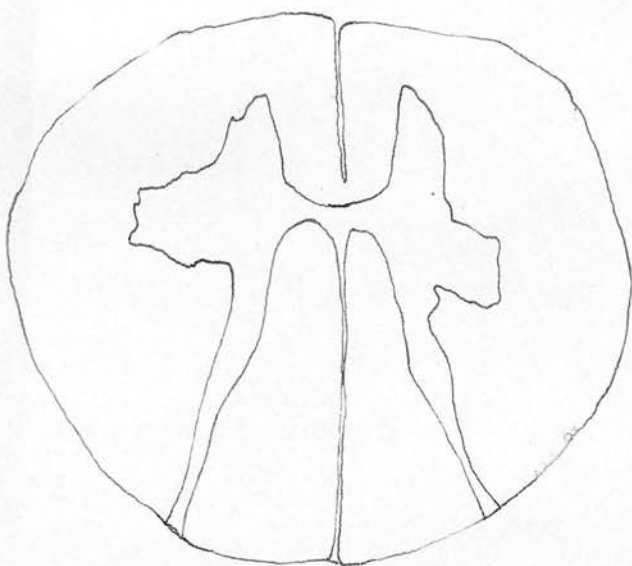
In the lumbar and upper sacral regions the posterior column was diminished in all its parts.

In the upper lumbar and lower dorsal region the best marked alteration was in the posterior column. Here, however, there was further a slight diminution in the number of cells in the column of Clarke e.g. in the region of the first lumbar root, a diminution in the proportion 122 to 99.

In the cervical region there was, as mentioned, a renewal of the atrophy in the postero-lateral ganglion cells, in the proportion 251 to 186. The atrophy could be traced to a short distance above the third cervical vertebra.

The second case was that of a man amputated through the right upper arm at the age of 40 years, who died ten years later. Here also there was a marked asymmetry of the cord affecting specially the cervical region due to a diminution both of the white

Marmesco



Case of amputation of the right upper arm:
Section from the first dorsal segment.
Outline tracing from Marmesco.

and the grey substance on the side of the amputation. In the lower and middle thirds of the cervical region the right half of the cord was less by a millimetre in diameter than the left. In the dorsal region this difference was reduced to half a millimetre and disappeared in the lower dorsal and lumbar region. Both the anterior and posterior roots in the cervical region presented an atrophied appearance. The atrophy of the white substance affected solely the column of Burdach.

In the right anterior horn in the cervical region there was a diminution in number of the ganglion cells affecting all the groups, not merely the postero-lateral. The right posterior horn appeared thinned, and the region of the anterior roots within the cord was atrophied. The alteration in the anterior horn extended as low as the first dorsal root, while the alteration in the column of Burdach extended somewhat lower.

There was likewise in the dorsal region, in this case a moderate diminution in the column of Clarke.

An examination of the nerves of the brachial plexus taken together gave the following result. Among normal fibres small bundles occurred composed of obviously atrophied slender fibres possessing almost

always an axis cylinder and a thin myelin-sheath. The contour of some of these fibres was not very sharp and it seemed that they must be on their way to complete disappearance, for on examination at corresponding levels it was found that on the amputated side the sum of the number of fibres was less than on the sound side.

In the third case the date of amputation and its duration were unfortunately unknown. The case was one of amputation through the left thigh.

In the lumbar region there was found a left-sided atrophy of the posterior roots, posterior horn and posterior column of white matter. The changes were not so marked as in the first case and there was no obvious alteration of the ganglion cells of the anterior horn. The column of Clarke on the left side was, however, somewhat atrophied.

An examination of the left sciatic nerve gave the following results. The normal myelinated nerve fibres were markedly diminished in their cross-section. The spaces between these fibres coloured deeply red with picrocarmine and contained extremely slender myelinated fibres; occasionally, however, the contour of the fibre in cross-section appeared uncertain and the myelin sheath entirely absent. The atrophy was much more marked in some parts of the sec-

tion than in others. There were also present fibres in which the axis cylinder was hypertrophied. In Marinesco's opinion the atrophy of the fibres may go on to complete disappearance and they may then be replaced by a moderate hyperplasia of the connective tissue and its vessels. As regards the spinal ganglions on the side of the amputation he convinced himself that many fibres had disappeared, while the ganglion cells appeared intact.

Finally Marinesco remarks, in regard to the atrophy of the posterior column, that in all three cases a close examination revealed the presence of slender fibres in greater numbers than normal in that region on the side of the amputation, and occasionally he was forced to conclude that the number of fibres was diminished, since the neuroglia showed no hyperplasia, a fact in his opinion worth remarking.

In his view the anatomical explanation of the various changes would be as follows. The bifurcation of the posterior roots on their entry into the cord explains the fact that atrophy of the posterior column occurred below as well as above the level of entry of the affected roots. The changes in the posterior roots explain the atrophy of the posterior column. The atrophy of Clarke's column may be explained in accordance with the researches of Flechsig

by its connection with the posterior roots. The atrophy of the anterior horn is explained by its connections with the posterior roots as demonstrated by Flechsig, Ramon y Cajal, and others. The atrophy of the anterior horn cells is more difficult to account for. To the theoretic conclusions of Marin-esco reference will be made later.

In 1892 Pellizzi in two cases of amputation of 10 and 11 years' duration respectively, observed atrophy of the posterior column together with atrophy of the anterior horn in its postero-lateral process and diminution in the number of its ganglion cells, in the corresponding portion of the cord.

In 1893 von Kahlden published a case of intra-uterine amputation at the elbow-joint with death from heart-failure at the age of 31. Hemiatrophy of the cord was present from the 4th cervical to the 2nd dorsal segment, constituted by a high grade of atrophy in both white and grey substances with the sole exception of the posterior column. In all the cell groups of the anterior horn a considerable diminution in number and a marked atrophy were present; in the postero-lateral group there were no cells remaining.

In 1894 Grigoriew investigated 5 cases. The first was that of a man aged 53 years amputated 20 years previously through the middle of the upper arm. At autopsy there were found cicatrised remains of two

hæmorrhages in the right and left halves of the cerebrum respectively. Upon section of the cord it could be seen macroscopically that there was a diminution in volume both in the white and in the grey matter on the side of the amputation in the entire course of the cervical region and in the commencement of the dorsal and a descending degeneration in the right crossed and the left direct pyramidal tracts could be traced as far as the 8th cervical segment. The descending degeneration was evidently due to the old hæmorrhage on the left side of the brain which had affected a portion of the internal capsule.

A detailed examination of the cord from the 3rd cervical to the 1st dorsal segment gave the following results: -

1). The nerve roots:— in the 3rd cervical segment, the left posterior root was somewhat smaller than the right; the anterior roots were equal in size. In the 4th segment, the left posterior root was less in circumference than the right in about the proportion of 4 to 5, and the left anterior root was somewhat smaller than the right. In the 5th segment, the proportion between the posterior roots became as 3 to 4, the single nerve fibres on the left side were somewhat more slender than on the right, and in Weigert preparations the myelin sheaths of a rela-

tively small number of fibres on the left side were seen to have undergone destruction; the proportion between the left and right anterior roots was 4 to 5. In the 6th and 7th segments, the left anterior and posterior roots were nearly equally diminished, in the proportion 2 to 3 as compared with the opposite side. In the 8th segment, the left anterior and posterior roots were diminished as compared with the sound side, the posterior more so than the anterior. In the first dorsal segment, the left anterior root was nearly equal to the right, but a decided difference still obtained between the posterior roots.

2) The white matter:— the antero-lateral columns were alike, the left posterior column was narrower than the right, especially in its anterior half, in the 3rd segment. In the 4th, the left antero-lateral column was somewhat smaller than the right. The left posterior column was about $\frac{1}{3}$ smaller than the right. In the 5th segment, the anterior and posterior columns were very obviously diminished on the left side, the posterior especially so, and the nerve fibres themselves appeared more slender than in the corresponding parts of the opposite side. In the 6th and 7th segments, the left anterior and posterior columns were about $\frac{1}{3}$ rd smaller than the right, and, in correspondence with this, the nerve fibres on the

left side appeared more slender and the interstitial tissue more rich in nuclei than on the opposite side. In the 8th segment, the anterior and posterior columns were diminished on the left side. In the 1st dorsal segment the left posterior column was diminished.

3). The posterior horns: 3rd segment; left smaller than right. 4th segment; left horn about $1/5$ th smaller than right. 5th segment; left horn smaller than right. 6th and 7th segments; left horn almost $1/3$ rd smaller than right. 8th segment; left horn smaller than right, but not so markedly, the entering bundles of the posterior roots could here be seen to be diminished as compared with the opposite side. 1st dorsal segment; the left horn somewhat smaller than the right.

4). The anterior horns: 3rd segment; almost equal in size, but on enumeration of the ganglion cells it was found that their number was somewhat diminished on the left side, along the median border of the horn and in the intermedio-lateral tract, in most sections; decided degenerative changes were likewise observed in single cells in these groups and elsewhere on the left side alone.

4th segment; the left horn decidedly smaller than the right, the diminution affecting partly the reticular process, the number of ganglion cells being diminished in all the groups, but especially along the median periphery of the horn where it amounts to $\frac{2}{3}$ only of the normal number (right side), and degeneration of ganglion cells occurring in all of them and amounting to $\frac{1}{3}$ of the cells along the median border. 5th segment; the left horn was strikingly diminished in all its parts and the projections of its contour smoothed away, the number of ganglion cells being much diminished, but especially in the median and lateral corners where scarcely half the cells remained, and atrophy of the cells themselves being marked in many of them especially in these two parts. The entering bundles of the anterior roots were less numerous and smaller on the left side, and the left reticular process was diminished in size. 6th and 7th segments; the left horn about $\frac{1}{4}$ smaller than the right, especially in its anterior half; the ganglion cells much diminished and very atrophic especially in the median and lateral groups. The anterior root bundles on the same side were less numerous and smaller and the processus reticularis was much diminished. 8th segment; no striking difference between the horns in size or

shape; the ganglion cells in all groups in the left horn were diminished and partly atrophic though to a less degree than above described. The left anterior root bundles were diminished in number and size.

1st dorsal segment; left horn slightly smaller than right; the ganglion cells not specially diminished but atrophic changes visible in many. The left anterior root bundles were slightly smaller than the right.

Below the first dorsal segment the results of examination were negative. It will be seen that apart from the degeneration of the pyramidal tracts the changes were unilateral and were best marked in the middle portion of the cervical region.

The second case was that of a man aged 32 years, who had had his right arm amputated 26 cm. from the shoulder 10 years previously in consequence of an injury inflicted by machinery. Death occurred from pulmonary tuberculosis. There had been no nervous symptoms. At autopsy the body was much wasted. Macroscopically, a diminution of the right half of the cord affecting both white and grey matter in the middle portion of the cervical enlargement could be noted.

Microscopical Examination:

Second and Third Cervical Segments: no alteration.

Fourth Segment: right anterior horn slightly smaller than left, and the ganglion cells slightly less numerous than on the right side and to a slight extent atrophic, especially along the median periphery and in the intermedio-lateral tract; right posterior horn slightly smaller than left, and right posterior root slightly more slender than left; right posterior column slightly smaller than left.

Fifth Segment: difference between anterior horns, uncertain; diminution in ganglion cells on right side very slight and few markedly atrophied ganglion cells present; right posterior horn and root diminished to an inconsiderable extent; the right posterior column of white matter was, however, about 1/5th narrower than the left.

Sixth and Seventh Segments: the right anterior horn decidedly smaller than the left; the ganglion cells decidedly diminished only in the median corner, but atrophy of ganglion cells visible in all the groups on the right side; the anterior root bundles smaller and less numerous than on the opposite side, and the reticular process less well developed; the right posterior horn decidedly reduced in size; the

anterior root on the right side very slightly, if at all, smaller, but the posterior root on that side about 1/5th smaller than the corresponding opposite root, many fibres appearing thinned, and certain fibres appearing degenerated, but in small number; the right anterior column of white matter somewhat smaller than the left, the posterior scarcely equal to 3/4ths of the left.

Eighth Segment: right anterior horn smaller than left, but to an inconsiderable extent; ganglion cells diminished throughout, although not strikingly so, and partly atrophied, especially in the median corner; the anterior root bundles somewhat smaller on the right side; the right posterior horn also somewhat diminished; the posterior roots on the right side inconsiderably diminished in size; the posterior column somewhat smaller on the right side.

First Dorsal Segment: the differences here were similar, but very slight in degree. Below this segment the cord appeared normal.

The third subject, aged 53 years, had, five years previously, been amputated through the inferior third of the thigh on account of a varicose ulcer in the leg. Death resulted from chronic Bright's Disease and pulmonary tuberculosis.

Macroscopically, the lower portion of the lumbar

enlargement on the amputated side appeared reduced in size to a quite unimportant extent.

Microscopically, from the 3rd to the 5th sacral nerve roots there were no changes in the cord.

In the 1st and 2nd sacral segments the left anterior horn seemed a little smaller than the right and the ganglion cells in the median and antero-lateral groups were diminished in number and partly atrophied. The left posterior horn was diminished to a slight extent, and the anterior and posterior horns on that side were slightly diminished. In the anterior columns there was no difference between the two sides, the left posterior column, however, seemed in its anterior part somewhat diminished.

Fifth Lumbar Segment: the left anterior horn was decidedly diminished, its ganglion cells were less numerous in all the groups, and part of them showed atrophic changes; almost $1/3$ rd of the cells in the median and ventro-lateral groups had disappeared, and about $1/2$ the remainder were atrophic. The anterior root bundles were somewhat smaller on the left side and the left reticular process seemed a little smaller. The left posterior horn seemed slightly smaller. The anterior and posterior roots were somewhat thinner on the left side and the left posterior column was somewhat smaller than the right.

Fourth Lumbar Segment: the left anterior horn was slightly smaller than the right with a diminished number of ganglion cells and atrophic changes in part of those remaining. The left anterior root bundles were somewhat diminished. The left posterior horn was slightly reduced in size. The left anterior root seemed slightly smaller than the right and there was a somewhat greater difference between the posterior roots. The left posterior column, especially in its anterior part, was decidedly smaller than the right.

Third Lumbar Segment: anterior horns equal in size, the ganglion cells in the left only very slightly diminished and only a small number of them showing atrophic changes. The left posterior horn was very much smaller than the right, the left posterior root only very slightly diminished and the left posterior column a little smaller than the right.

Second Lumbar Segment: the only changes on the left side were a very slight amount of atrophy in the ganglion cells of the median and ventro-lateral groups and a very slight diminution of the posterior root.

From the first lumbar segment upwards the only change observed was in the ganglion cells of Clarke's column, which, as far as the 10th dorsal segment,

showed a diminution in their number and a slight atrophy on the left side.

Examination of the Sciatic Nerve: The changes here observed were diminution in number and size of the nerve fibres, and alterations in diverse grades of the myelin sheath, e.g. thinning, feeble colouring, or almost complete loss of colouring power, and granular disintegration, together with an increase in the nuclei and in the interstitial connective tissue. About half the fibres in each bundle showed the alterations above mentioned.

The fourth case was that of a woman aged 23 years amputated two years previously through the middle of the left leg on account of a tuberculous inflammation of the ankle joint. Death ensued from pulmonary tuberculosis. The only changes found in the cord were in the fourth and fifth lumbar segments, in which the posterior roots and posterior column on the side of the amputation were very slightly smaller than on the opposite side.

The fifth case was that of a patient aged 47 years, amputated a year previously between the middle and inferior thirds of the right thigh on account of a tuberculous inflammation of the knee. Death resulted from pulmonary tuberculosis. No changes of any sort whatever were found in the spinal cord.

Grigoriev sums the results of his investigations as follows. In four out of five cases the cord showed changes, which invariably affected the side corresponding to the amputation and were of the same character throughout. The degree of the alterations bore a direct relation to the number of years elapsed since the amputation, and they were localised exclusively in the nervous elements of the cord. Finally both the motor and the sensory apparatus were affected, the sensory to a more marked degree.

In 1897, Sibelius investigated the case of a man amputated just above the left knee at the age of 65 years. Death from pneumonia occurred at the age of 70 years. He is stated to have observed the following alterations. The anterior horn cells in the lumbar enlargement were fewer on the amputated side, the diminution occurring chiefly in the postero-lateral group. The changes in the anterior nerve roots were unimportant. In the segments corresponding to the limb removed, and on the side of the amputation, some of the nerve cells in the ganglia of the posterior roots had disappeared and others had atrophied. The left posterior column in the same region showed distinct atrophy with rarefaction of the nerve fibre bundles and the course of this atrophy in the cord corresponded to that of posterior roots derived from

the affected segments.. The reflex collaterals were diminished in number on the same side and the cells of Clarke's column on that side were diminished in number.

Sibeliu8 regarded these changes as resulting from the injury to the axis cylinders in the divided nerve.

Elzholz found in the central end of the divided nerves (2 cases), after several years, a diminution in size of the large medullated fibres as these descended into the stump which was due solely to a thinning of their myelin sheaths, while at the same time there was a progressive diminution in the number both of large and of small medullated fibres. Non-medullated nerve fibres appeared in increasing numbers as the extremities of the divided nerves were approached, arising to all appearance out of the small medullated fibres.

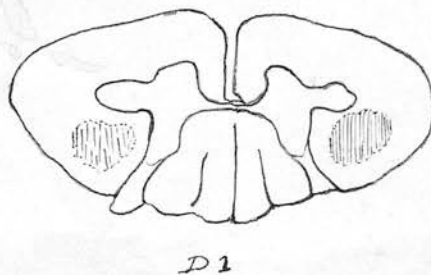
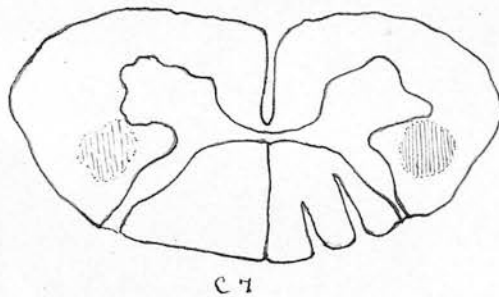
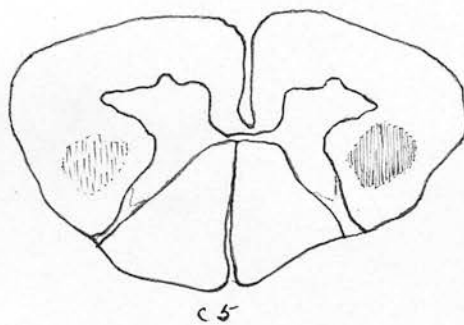
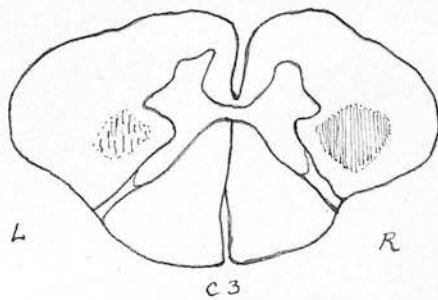
In 1901, Barratt published the results of his examination of a case of long-standing amputation. The subject had been amputated at the age of 19 years through the middle of the right upper arm. Death occurred at sixty-one years of age. For six years before death mental changes had been evident, including an attack of suicidal depression and finally failure of memory and dementia. At the time of death

the muscles of the shoulder were wasted to an extreme degree. At autopsy a condition of senile atrophy of the brain was determined, with general wasting of the mantle, and an old softening on the left side involving the apex of the cuneus and adjoining lingual convolution, extending forwards to the ependyma of the lateral ventricle and posteriorly to the optic radiations.

The spinal cord showed right-sided atrophy in the cervical region; there was no obtrusive difference in the aspect of the nerve roots.

The hemiatrophy of the cord was strongly marked from the 2nd to the 6th cervical segments, less marked in the 7th and 8th segments, slight in the 1st and 2nd dorsal segments, and below this indistinct. In the white matter there was some wasting of the right posterior column in the whole cervical region and in the first dorsal segment. No marked sclerosis was here recognisable. There was further a diminution in the antero-lateral column on the right side, traceable to the 10th dorsal segment, and gradually diminishing, which seemed to be due to a sclerosis in the crossed pyramidal tract. A similar, but much slighter, sclerosis was present on the opposite side, extending to the 8th dorsal segment. The anterior horn was diminished in the cervical region, and the

Barratt



Barratt.

1st dorsal segment on the right side, and its ganglion cells, especially in the outer part of the horn, diminished in number and size from the 5th to the 8th cervical segment and slightly in the 1st dorsal, the proportions being roughly 83 to 100 as compared with the opposite side. The right posterior horn was not apparently wasted. The posterior root ganglia presented nothing special in so far as they could be compared.

In the medulla, the left anterior pyramid was much wasted as compared with its fellow, and the left half of the whole section was smaller than the right. The olivary bodies were of nearly equal size. The atrophy of the left pyramid could be followed into the mesencephalon and further asymmetries were observed in the brain, but the condition of that organ makes their interpretation uncertain. No difference was discernible in the cortex between the right and left hand and forearm areas. It should be noted that there was no marked difference between the gracile and cuneate nuclei on either side of the medulla. The left optic thalamus was smaller than the right.

Barratt notes that "the hemiatrophy did not correspond in degree to the extent which the relation of spinal segments to body areas would suggest." Thus C.8 and D.1 were less affected than the segments

immediately above. The diminution in size and number of the anterior horn cells corresponded closely to the amputated member.

In 1905 Léri published an account of his examination of 12 cords from amputated patients. Of these, nine were from patients amputated through the thigh, one from an amputation through the leg and two were from amputations through the forearm. He discussed simply the degenerative lesions which he observed in the posterior columns, without going into much detail. In correspondence with the observations of Marie, the lesions were of the nature of a ~~true~~ sclerosis and especially clear, as was natural, in the column of Goll in the cervical region. They were more marked on the side of the amputation, but existed nevertheless in both posterior columns. The homolateral lesions were extremely variable, e.g. certain amputations through the thigh had produced lesions less marked than that produced by the amputation through the leg. The heterolateral lesions were likewise of very variable extent, in some cases scarcely marked, and in others almost as clear as those on the side of the amputation. He considers this variability as an argument against the view that the lesions are produced by simple trophic trouble. Again, in two long-standing cases, dating back 71 and 45 years respectively,

the degenerations were very well marked, but in some much more recent cases (dates not given, however) they were at least as obvious. In several cases suppuration had occurred in the affected limb either before or after amputation, but the alterations were not sensibly more marked than in the other cases. In two cases, one certainly syphilitic and the other suspected to be so, he observed a very intense meningeal lymphocytosis. In both, the lesions were much more marked on the side of the amputation, in one among the most intense observed, in the other among the least marked. In the meninges of several other cases he thought he could observe remains of meningeal inflammation. In his opinion a hypothetic meningitis, presumably due to an ascending neuritis spreading from the amputation stump, would explain the variability of the changes observed in the cord.

In 1909, Déjérine and Madame Déjérine published a case of right scapulo-humeral disarticulation at the age of 4 years, with death at the age of 48. Their object was the study of motor localisations. On examining the cord, they observed a hemiatrophy of its right half, affecting in the white matter chiefly the posterior column and particularly the column of Burdach. In the grey matter both anterior and posterior horns were affected with a diminution in the number

of their cells and an alteration in the character of these. As regards the anterior horn, its antero-lateral ganglionic column conformed sufficiently, in its atrophic changes, with the results of experiment, and of observation in medullary diseases. In the postero-lateral column, however, the presumed centres for the forearm and hand were remarkably rich in cells. The same held good for the centres for the biceps and triceps. The centres for the brachialis anticus and the muscles of the shoulder showed a considerable diminution. The antero-lateral column for the muscles of the back and neck showed likewise a considerable reduction as high as the 5th cervical segment.

The authors concluded that the cords of amputated persons are not favourable material for the elucidation of spinal motor localisations, and propose the degree of proliferation, in the amputation neuromas, of the fibres proceeding from the cells, as the determining agent in the conservation of the latter.

In illustration of the foregoing account the following cases may be of interest: -

- 1) Mimey: amputation through the inferior third of the left thigh for tuberculous arthritis, 3 years previous to death.

- 2). Minost: Amputation through the inferior portion of the right leg for a crush of the right foot, 60 years previous to death.
- 3). Gasnier: Amputated through the inferior third of the right thigh. Duration of the amputation unknown.
- 4) Raoult: Lisfranc's amputation of the left foot for contracture following on infantile paralysis, 16 years previously to death.
- 5). Besnier: Numerical atrophy of the left lower extremity following on an ankylosis of the knee at the age of four years. Death at 65 years of age.
- 6) Durand: Infantile paralysis at the age of 16 months with much resulting atrophy of the left leg.

N.B. For Illustrations see the end.

Case 1.

Mimey: Amputated through the inferior third of the left thigh for tuberculous arthritis in November 1905. An arthrotomy was first done in June 1905. Died of pulmonary tuberculosis in November, 1908.

Duration of the amputation 3 years.

An examination of the accompanying drawings reveals the following conditions: - In the 1st, 2nd, 3rd, 4th and 5th lumbar segments there is marked asymmetry of the posterior columns of white matter, the smaller of the two being upon the side of the amputation. A similar marked asymmetry of the posterior

horns is noticeable in the 2nd, 4th and 5th lumbar segments. In the 3rd, 4th and 5th lumbar segments the left anterior horn is decidedly smaller than the right. On the other hand in the second lumbar segment the right anterior horn is the smaller of the two. In the dorsal and cervical regions there are no very striking alterations. Note, however, the appearance about the second dorsal segment of a slight degeneration or sclerosis, best seen in the third cervical segment (first and second not examined), slightly more marked on the side of the amputation, and visible in the cervical segments shown, both in the column of Goll and in the column of Burdach.

Case 2.

Minost: Amputated in 1849 for a crush of the right foot, died in 1909.

A noticeable atrophy of the right leg existed, especially of the muscles of the calf. The atrophy of the thigh was less marked, except in the case of the rectus muscle. Duration 60 years.

Unfortunately the lumbar and sacral segments of the cord were destroyed.

Note the marked diminution in size of the right posterior column of white matter as compared with the left, very readily seen in the 8th cervical and first

dorsal segment. Note further a sclerosis in the posterior columns in the column of Goll, more marked on the side of the amputation and becoming more distinct up to the 1st cervical segment.

Case 3.

Gasnier: amputated through the inferior third of the right thigh, date unknown. Died at Bicêtre, 1909.

Regarding this patient no further information was obtainable. Previous to his death there were no tabetic symptoms.

Note a well-marked diminution in size of the right posterior column, as compared with the left, particularly in the lumbar and sacral regions, but sufficiently obvious in the cervical region. Note likewise a very marked degeneration of the posterior columns, particularly on the side of the amputation, observable throughout the cord and confined in the cervical region to the column of Goll. The posterior roots examined in the sacral region showed a marked degeneration of their fibres on both sides of the cord, but much more so on the right side. There was no asymmetry in the medulla.

Here it seems very probable that the sclerosis was in reality tabetic. It is, however, interesting to note its considerably greater severity upon the side of the amputation.

Case 4.

Raoult: At the age of 5 years an attack of poliomyelitis anterior acuta, affecting the left lower limb. Contracture followed and the foot became completely twisted so that he was obliged to walk upon its outer side. In 1893 when he was 26 years old Lisfranc's operation was performed. In 1903 he entered Bicêtre. At this time there was a considerable atrophy of the left leg and also an atrophy, less marked but very evident, of the left thigh. He could however carry out any movement at the knee and hip. The circumferences of the calves were as 31 to 23, those of the thighs as 40 to 33. The lengths of the lower limbs to the external malleolus were equal. Death occurred at the age of 42. This patient presented also some very interesting functional nervous peculiarities and in this connection the case has been described by Raymond and Janet in the *Nouvelle Iconographie*, 1902, p. 241.

Note the atrophied condition of the left anterior horn in the 2nd, 3rd, 4th and 5th lumbar segments, and in the first sacral segment. The left posterior column is smaller than the right, the difference being specially marked near the grey commissure. There is a similar difference between the posterior horns in the 3rd, 4th and 5th lumbar segments, especially the

3rd. Lastly there is a definite degeneration in the cervical region in the column of Goll, slightly more marked on the side of the amputation.

Case 5.

Besnier: Since the age of 4 years the left knee has been ankylosed in flexion, in consequence, probably, of tuberculosis. In consequence of this the left leg never developed like the other. It was shorter than the other and partially atrophied. From the age of 40 years onwards the atrophy of the muscles became gradually more marked. Death occurred at the age of 65 years.

Note a diminution in size of the left posterior column as compared with the right, especially near the grey commissure, extending from the 4th lumbar segment to the middle dorsal region. The anterior horn on the left side is perhaps slightly diminished in size in the lumbar region. Note further a degeneration in the posterior columns best marked on the side of the atrophied limb, appearing first in the upper dorsal segments near the grey commissure, and becoming gradually more obvious in the column of Goll in the cervical region.

Case 6.

Durand: Infantile paralysis at the age of 16 months with much resulting atrophy of the left leg. The left arm also was stated to have been completely paralysed, but to have gradually recovered and from the age of 21 years onward it was possible to use it, and at present it is almost as strong as, and no smaller than, the right. Death at the age of 52 years.

Dimensions of the lower limbs: -

Circumference of thigh; R. 45 cm., L. 33 cm.

Circumference of calf; R. 31 cm., L. 22 cm.

Length of limbs; R. 80 cm., L. 69 cm.

The left foot was clubbed, - equino-varus. The right leg appeared practically normal.

Note the lesions as shown by white, or comparatively lightly shaded, outlined patches and the atrophy of the left anterior horn in the fourth lumbar segment. Note further a slight but definite sclerosis in the columns of Goll, beginning about the middle of the dorsal region. The posterior columns are asymmetrical, but the asymmetry is not constant.

In proceeding to discuss the preceding observations it will be convenient to deal first with the changes affecting the peripheral nerves. In regard to these the observations of authors are on the whole concordant. With the exception of Vulpian (2 cases)

alterations similar in character were observed in the nerves studied. These consisted generally in the appearance of an unusually large number of slender fibres to all appearance atrophied, frequently fasciculated, and extending from the neuroma in the stump for a varying distance towards the spinal ganglia. Authors differ, however, in their interpretations. Hayem and Gilbert observed appearances indicating in their opinion a re-growth of previously degenerated fibres. Vaulair and Marie held a similar view and the observations of the latter seem to justify it in a high degree. On the other hand those of Dickinson, Déjérine and Mayor, Homén, Marinesco and Elzholz pointed in the opinion of these authors towards a simple atrophy. There can be little doubt in fact that such an atrophy occurs although probably to a varying extent in different subjects. It may be noted further that atrophy and regrowth of fibres are not mutually exclusive, and it is not unlikely that both may occur in the same nerve-trunk particularly in the neighbourhood of the stump.

As regards the spinal ganglia, most authors have refrained from offering an opinion, chiefly on account of the technical difficulties which attend the comparison of these on either side of the cord. Brown Séquard, however, mentions a diminution in size on the

affected side (1 case) and Homén's observations are in agreement. A comparison of the spinal roots has likewise been found to be a matter of difficulty, particularly in the cauda equina. Unilateral atrophy has, however, not infrequently been described, and most often in the posterior roots.

The alterations in the cord itself present a very striking amount of variation from one case to another. It will be noted, however, that these differences are much less marked in the comparatively recent as compared with the earlier accounts; a fact which makes it probable that some at least of the earlier divergencies are to be attributed to defective technique. It results in any case from a total comparison that the posterior columns and the anterior horns are those parts which are most constantly and most markedly affected, that is to say, those portions of the cord which are in the most direct functional relation with the affected limb. Further, all authors are agreed that the lesions are best marked in the lumbar enlargement in cases of amputation of the lower limbs and in the cervical in cases of amputation of the upper and that they are unilateral. The exceptions to the last remark consist in the scleroses in the posterior columns described by Marie, Pellózzzi, and Léri, and occurring also in my cases to varying extents.

In explanation of the facts observed divergent explanatory hypotheses have been offered. The opinion of Flechsig that the asymmetry observed was always congenital cannot now be considered tenable. Certain authors have sought an explanation in a supposed inflammatory process, spreading along the nerve-trunk from the stump, but no inflammatory lesions of consequence have been observed and the systematised nature of the process makes the explanation improbable.

Dickinson, Friedreich, Hayem, and Gilbert, supposed that the section of a nerve might result in persistent irritation of the cells of the cord through the cylinder axis and that the medullary alterations might thus be produced. Vulpian and Edinger considered that the atrophy was the result of the functional inertia imposed upon the nerve elements by the operation. In support of this Vulpian described a case of ankylosis of the elbow, in which he found an atrophic alteration in the corresponding anterior horn. The theory of Krause and Friedländer in reference to the supposed function ascribed by them to specific sensory nerve-endings in maintaining the integrity of their fibres has already been mentioned. Further research, however, has failed to bear it out. Moreover they were undoubtedly mistaken in supposing sensory tracts ^{to be} ^{affected} alone. Vanlair believed that the changes in the cord in man

ought to be considered rather as the result of the surgical affection necessitating the amputation, than of the amputation itself. Marie, while believing in a direct relation between the changes in the cord and the amputation, has no theory to offer apart from his opinion that certain sensory fibres have their trophic centres at the periphery and not in the spinal ganglions. Marinesco concluded that the alterations in the nerves and cord varied inversely with the age of the subject at the time of operation and directly with the length of life afterwards, and that they were undoubtedly due to the breakage of relations between the centre and the periphery. He considered that the normal stimuli which traverse a sensory nerve are essential to the maintenance of a sufficient trophic activity in its ganglion cells. He thought it possible that the spinal ganglion cells might remain comparatively intact, while this supposed diminution in their activity resulted in atrophy of their processes. Since an atrophy was clearly demonstrated in the motor ganglion cells of the anterior horn, he concluded that these were specifically less resistant than the cells of the spinal ganglions. The conclusions of Grigoriew are on the whole in accordance with those of Marinesco. With regard to the changes in the motor realm Déjérine and Madame Déjérine propose

the degree of proliferation of the fibres in the amputation stump as the possible determining agent in the conservation of certain groups of cells as compared with others in the case which they examined.

Turning now to the experimental pathology of the neurone as it has been worked out in recent years, we find the facts to be in favour of Marinesco's view. In 1896 Lugaro described the changes that occur in the ganglion cells of the anterior horn after section of the sciatic nerve as follows: - In the first or reactive phase he observed a chromatolysis commencing in the origin of the axis cylinder. In the second or degenerative phase the chromatolysis extended to the greater part of the cell body and the nucleus was displaced. Finally the chromatolysis advanced into the protoplasmic processes, the entire chromatic portion assumed a powdery appearance and the delicate striation of the achromatic substance was completely lost. From an examination of the same tissues with Golgi's method he concluded that it is only with the commencement of destruction of the cell (degenerative phase) that alterations become recognisable by this method. Further by similar experiments upon the cells of the spinal ganglia he was able to demonstrate that although these cells undergo marked chromatolysis after section of their peripheral prolongation they are not

affected by section of their central branch. He explained this difference by supposing that the sensory element resents especially the suppression of external stimuli, the motor element the suppression of its discharge of energy. Van Gehuchten has described two stages in the changes which occur in the motor cells of the spinal cord after section of their nerve fibres; the first, a stage of chromatolysis and the second a stage of restitution. He believes that the amount of cell-destruction which occurs is in reality very slight, and to be attributed to loss of the nucleus from excessive swelling of the cell. On the other hand he stated that in the cells of the spinal ganglia reconstruction does not occur, but complete degeneration, and he attributes this difference between the cells to the fact that the sensory cell is deprived of its physiological excitement while the motor cell is not. In 1899 Marinesco, on the ground of his own experimental observations, defended his previous conclusions upon these points. Finally it has now been fully proved (Monakow, Dotto and Pusateri, Ceni, Ballet and Faure, Marinesco) that the large pyramidal nerve cells of the cortex undergo secondary degeneration proceeding often to complete destruction after injury to their axis cylinders.

On the whole then I think it must be admitted that the view originated by Vulpian and defended by

Marinesco which ascribes the changes observed to the functional inertia of the affected neurones, as well as of their immediate associates, e.g., the cells of the column of Clarke in the sensory system, is that which is best supported by the evidence at our disposal. The effects of disuse are well known in regard to the nutrition of the various tissues of the body. The nervous system is then no exception to the rule. The variety observed in the intensity and distribution of the lesions may be accounted for in various ways. Possible defects of technique among the earlier observers have already been referred to. In some of his cases Vulpian found that the cord was affected by asymmetry to an almost equal extent throughout its length. Certain fixing and staining processes produce a considerable change in the dimensions of the section, in particular, perhaps, those which involve the application of heat. The actual cause of the amputation, e.g. the tearing or crushing of an extremity, may very well influence the rapidity with which the subsequent changes in the nervous system develop. It is a well-established fact that a *réaction à distance* in the spinal centres is more rapidly produced experimentally by tearing away a nerve than by cutting it through. According to Oppenheim the progress of *tabes dorsalis* may be materially hastened by an injury to an affected

limb. Again the traumatic neuroses furnish evidence of the extent to which the nervous elements may be functionally affected by shock and therefore presumably their nutrition altered. Most authors are agreed that the younger the subject the more marked are the alterations found, and this is strikingly illustrated by the results of Homén's and Vaulair's experiments upon young and upon adult dogs, the former finding well marked changes, and the latter none of any consequence. All authors who have had an opportunity of making the comparison are agreed that the longer the time elapsed since the amputation the more obvious are the alterations. Again the resistance of the nervous elements to decay probably varies considerably from one individual to another and probably from one group of elements to another in the same individual. In this way may be explained the variety of the cell groups principally affected by the atrophy in the anterior horns, although it may appear that of these the postero-lateral group shows a peculiar disposition to degenerate (Friedländer and Krause, Homén, Marinesco). That senile regressive changes occur in the nervous elements seems to be well established, as well as that they do not affect all the nerve cells in an equal degree (Hodge, Pognat, Marinesco). Luzenberger concluded from his observations upon the guinea-pig that

even under normal conditions a certain number of nerve cells undergo a regression which ends in their complete destruction.

With regard to the origin of the scleroses in the posterior columns described by Marie, Pellizzi and Lévi and occurring likewise in my cases I have no decided opinion to offer. That they are not of constant occurrence appears certain. In one of my cases (case 3) the sclerosis was, as already noted, probably tabetic. In case 1, the sclerosis, slight in itself, was as obvious in the column of Burdach as in the column of Goll. In case 2, the lower portion of the cord was not examined. Assuming these degenerations to be accidental, it is not surprising in the light of what has been said already, that they should be more marked upon the side of the amputation. A priori, however, there is nothing impossible in the supposition, that in certain cases the atrophy may proceed so far as to destroy completely a sufficient number of fibres to constitute a true sclerosis. It is remarkable that in the case of pure atrophy of the lower limb (Case 5), which was originally examined for purposes of comparison, there should be so well marked a difference between the posterior columns. This might be supposed to be due to a destruction of sensory fibres in the atrophied muscles of the limb, but

case 6 fails to bear out this assumption.

To sum up: - The changes in the nervous system after amputation may be regarded as the result of trophic disturbances in the immediately affected elements, particularly those which are sensory in function and thus immediately deprived of their natural stimulus to activity. They at least are usually first affected, though after a longer or shorter interval changes in the motor cells, and by consequence in their axis cylinders, also result.

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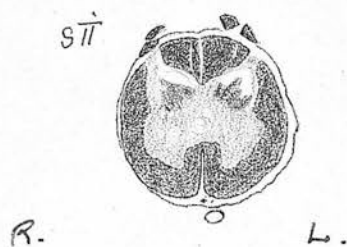
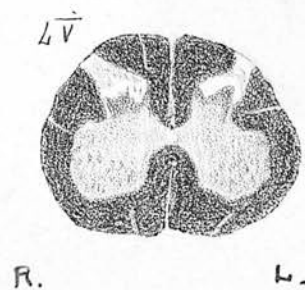
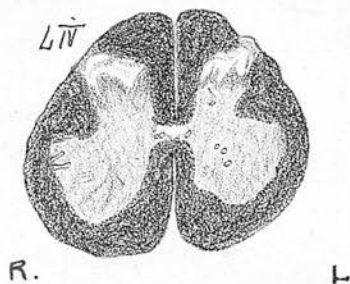
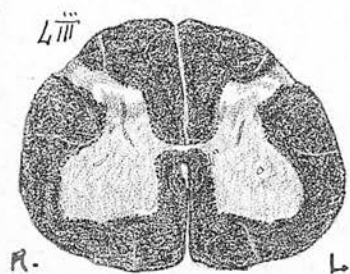
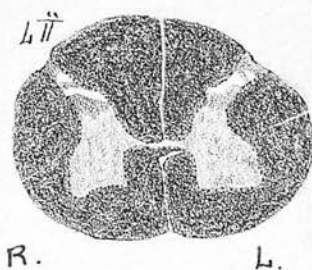
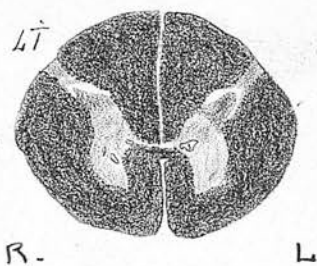
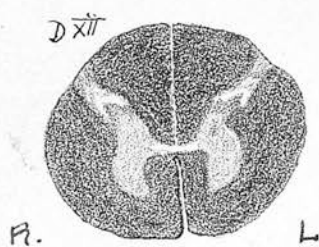
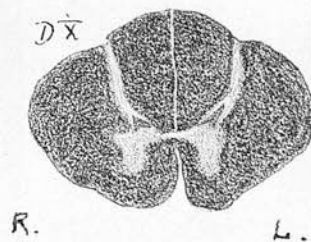
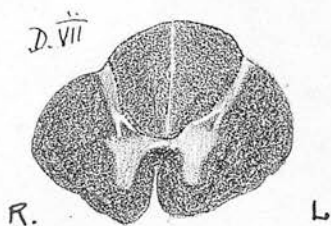
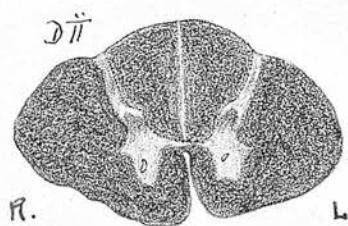
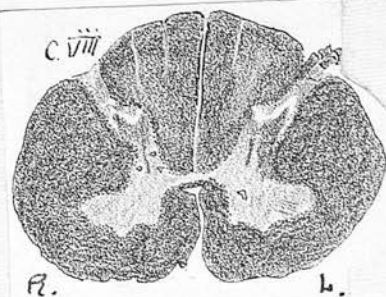
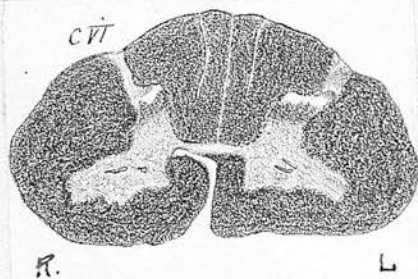
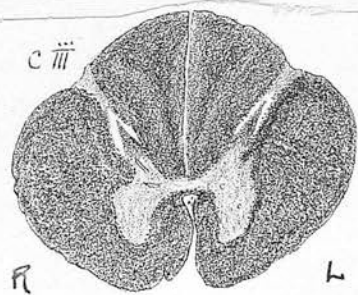
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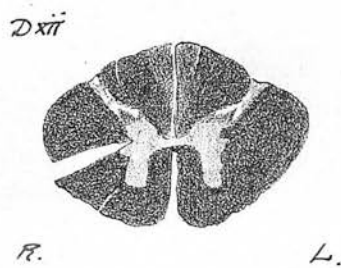
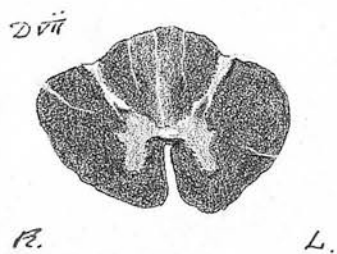
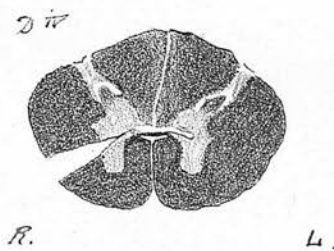
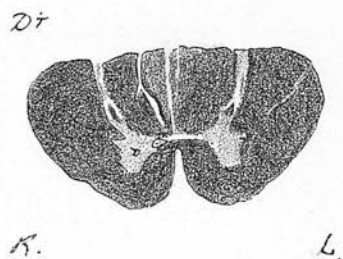
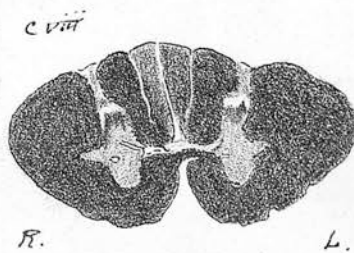
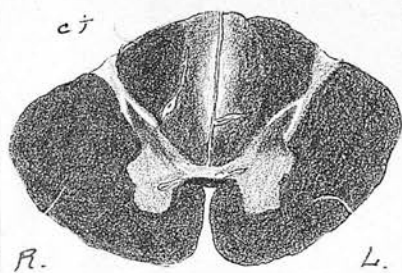
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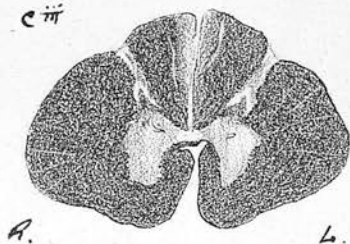
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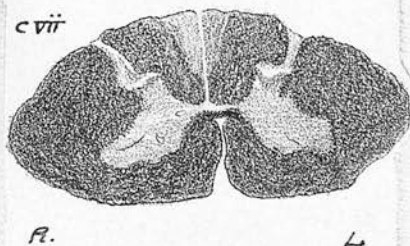
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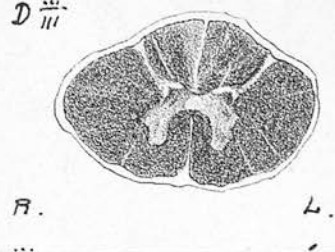
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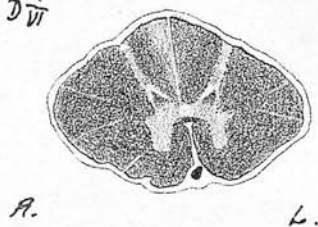
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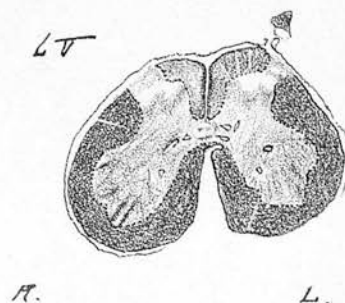
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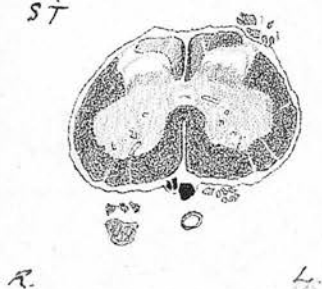
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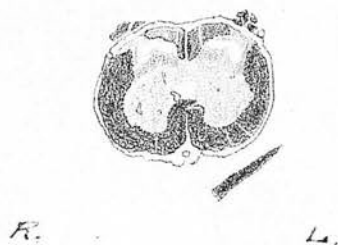
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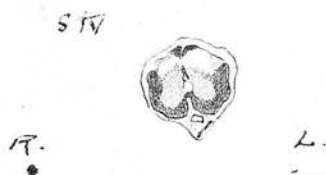
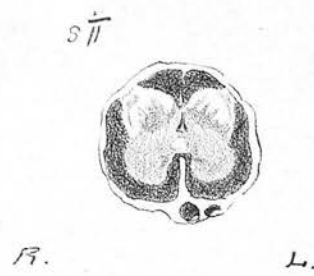
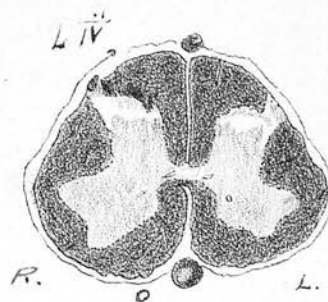
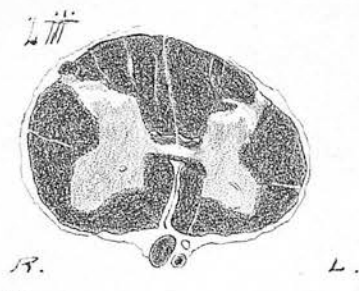
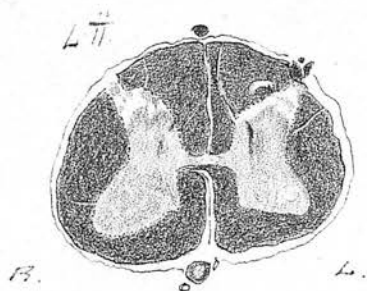
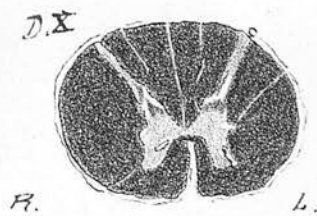
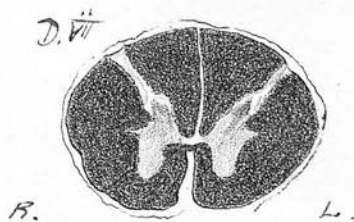
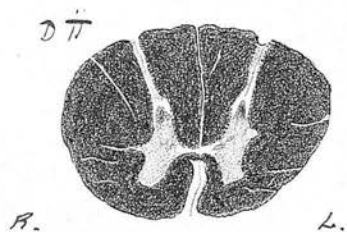
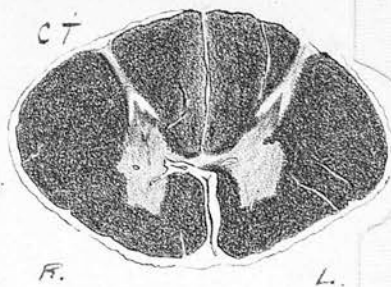
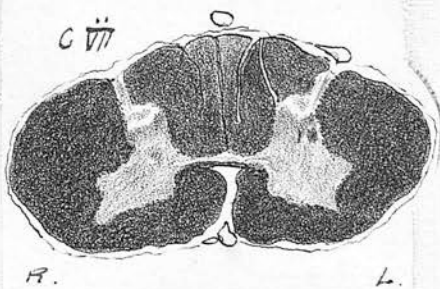
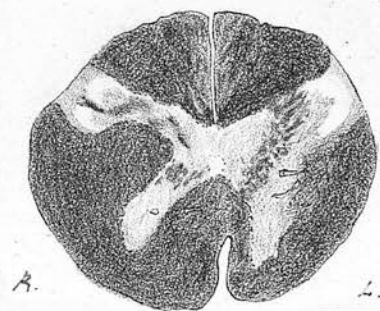


S II



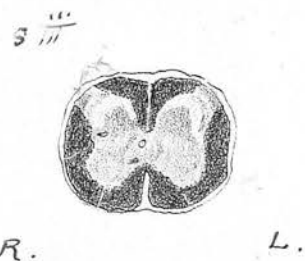
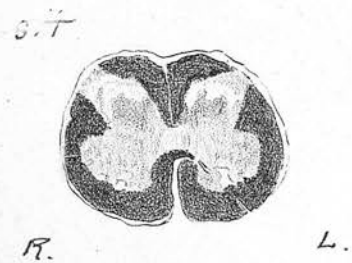
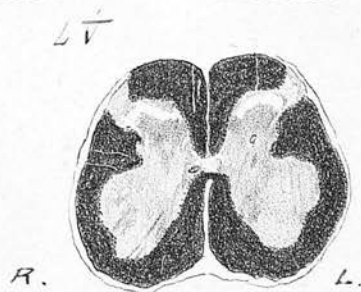
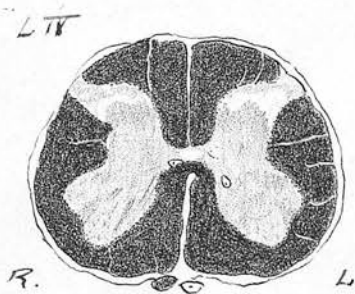
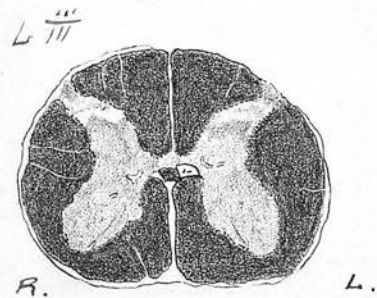
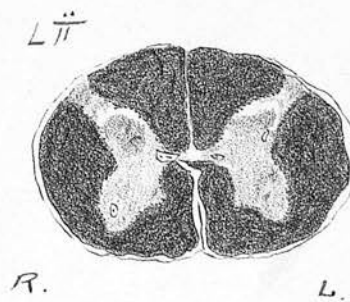
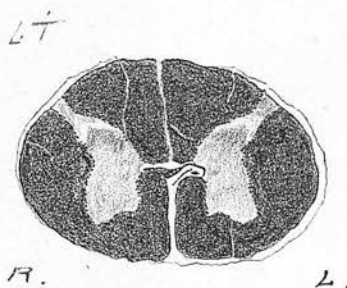
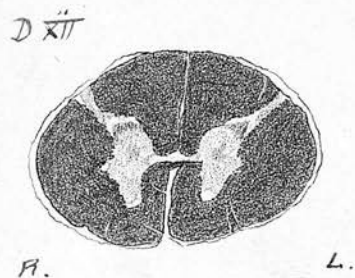
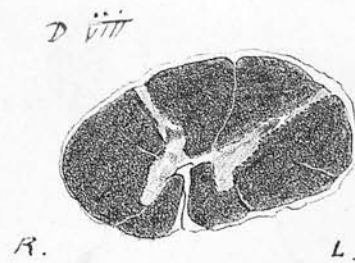
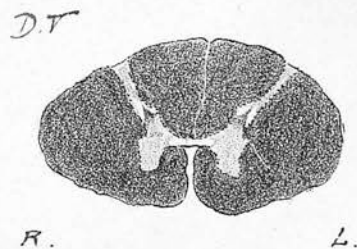
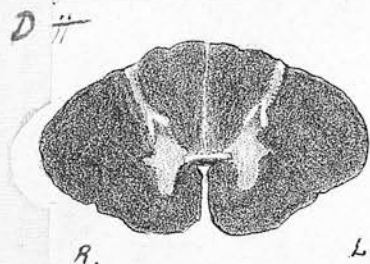
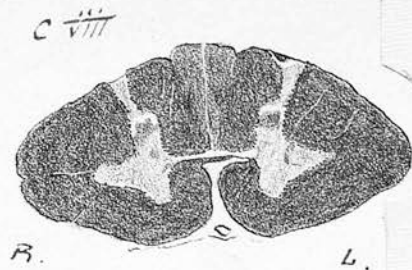
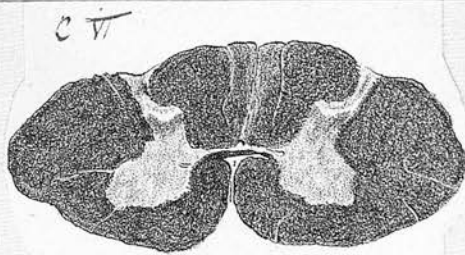
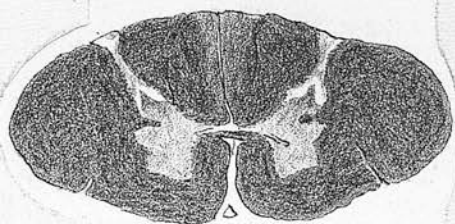
Case 3)

Gasmier.



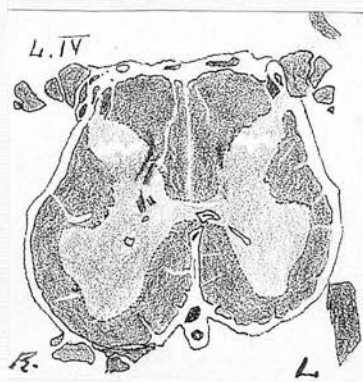
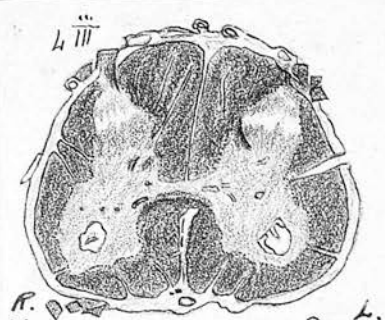
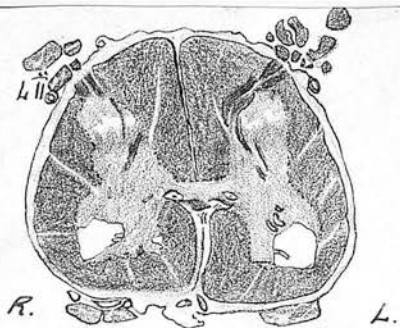
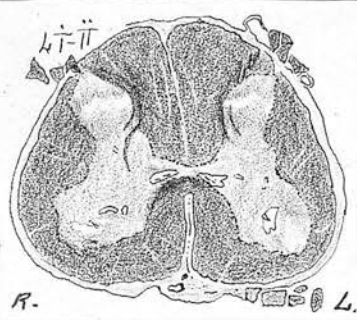
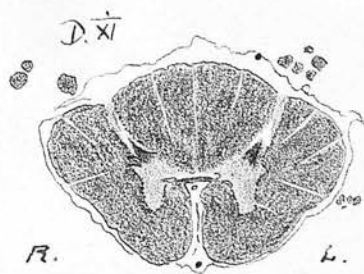
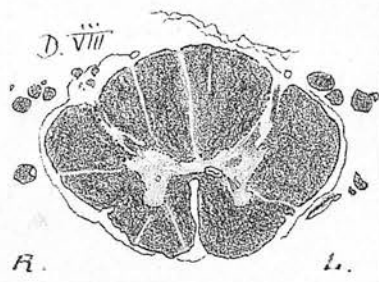
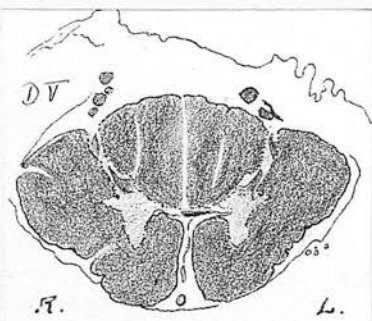
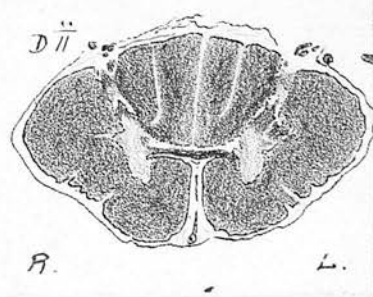
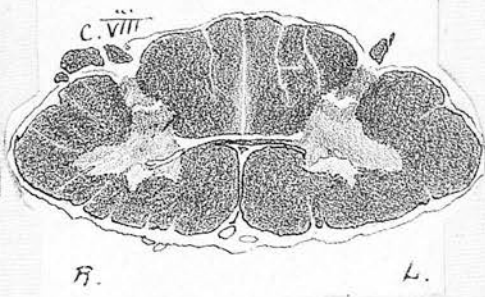
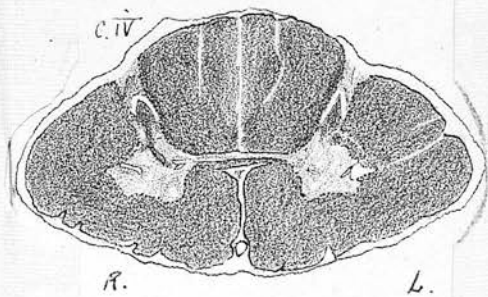
Case 4)

Raoul.



Case 5-)

Besmer :



Case 6. Durand: